1.0 PURPOSE

The purpose of this policy is to ensure that all clinical research sites conduct Division of Acquired Immunodeficiency Syndrome (DAIDS) funded and/or sponsored clinical trials in accordance with the requirements and regulations for human subject protection and the use of investigational new drugs.

2.0 SCOPE

This policy applies to all clinical trials funded and/or sponsored by DAIDS. This policy also applies to observational studies performed with DAIDS funded and/or sponsored HIV/AIDS Clinical Trials Networks and network collaborators.

3.0 BACKGROUND

DAIDS has an established protocol registration process in place for all clinical research sites to register their participation in DAIDS funded and/or sponsored clinical trials. The protocol registration process ensures that site-specific informed consents contain the necessary information to comply with Federal Regulations. This includes the required basic and additional informed consent elements as outlined in the Office for Human Research Protections (OHRP) 45 CFR 46 and the Food and Drug Administration (FDA) 21 CFR 50 (for IND studies). In addition, the protocol registration process verifies that clinical research sites provide the necessary Institutional Review Board (IRB)/Ethics Committee (EC) approvals and all documentation required by the FDA or DAIDS regarding investigator qualifications and responsibilities. The protocol registration process has been extended to include all DAIDS funded and/or sponsored clinical trials, irrespective of number of participating sites, or funding mechanism.

4.0 DEFINITIONS

Clinical trial – a prospective study of human subjects designed to answer questions about biomedical or behavioral interventions, e.g., drugs, treatments, devices, or new ways of using known treatments to determine whether they are safe and effective.

DAIDS sponsored – DAIDS is responsible for the management (including submission of the Investigational New Drug Application (IND) to FDA, and initiation of the study), and oversight for the trial**.**

DAIDS funded – DAIDS is providing financial support for trial or study.

Investigator of Record (IoR) – the person responsible for the conduct of the clinical trial at a clinical research site. This person is the signatory for the Form FDA 1572 (IND studies), or DAIDS IoR Agreement (Non-IND studies).

Principal Investigator (PI) – the qualified person designated by the applicant institution to direct the funded research program. PIs oversee the scientific and technical aspects of a grant and the day-to-day management of the research.

Regulatory Affairs Branch (RAB) – a branch of DAIDS within the Office for Policy in Clinical Research Operations (OPCRO). RAB performs regulatory surveillance over clinical trials funded and/or sponsored by DAIDS.

Regulatory Compliance Center (RCC) – a contract based organization charged with providing regulatory support to RAB, DAIDS.

Protocol Registration Office (PRO) – an office within the RCC that receives and processes all protocol registration materials for DAIDS.

Scientific Review Committee (SRC) – a reviewing body instituted by DAIDS to review the concepts and protocols developed by various programs within DAIDS.

For additional definitions see DAIDS glossary.

5.0 RESPONSIBILITIES

IoR/PI – After receiving final IRB/EC approval of the protocol and site-specific informed consent, the IoR/PI will ensure that their clinical research site submits all the required protocol registration documents to the PRO.

Program Officer – At the time of grant award, for Non-network trials, the Program Officer will inform the IoR and PI of the need to complete the protocol registration process and will provide various tools, templates, the RCC website, and the current DAIDS Protocol Registration Policy and Procedure Manual to assist the IoR/PI in protocol and site-specific informed consent (IC) development.

RCC/RAB – The PRO at the RCC implements and manages the day-to-day operations of the protocol registration process. All required protocol registration documents are submitted to the PRO. RCC personnel, under DAIDS-RAB oversight, review the registration materials.

6.0 POLICY

6.1. All clinical research sites are required to complete protocol registration for all clinical trials in accordance with current DAIDS Protocol Registration Policy and Procedures Manual prior to enrolling any participants. This also applies to observational studies performed with DAIDS funded and/or sponsored HIV/AIDS networks and network collaborators. The most current version of the DAIDS Protocol Registration Policy and Procedure Manual is available on the RCC website for all clinical research sites to assist them in completing the steps for protocol registration.

6.2. DAIDS Protocol Development Requirements Before Protocol Registration Can Occur:

6.2.1. SRC Review - DAIDS via the RCC sends a SRC summary letter, which includes comments related to the protocol and informed consent. These comments must be addressed before full regulatory review.

6.2.2. Regulatory Review - After the final SRC review, the protocol and informed consent will undergo a full regulatory review conducted by the RCC/RAB. Final regulatory comments are issued upon completion of the review. These comments must be addressed before final Medical Officer review/sign-off.

6.2.3. Medical Officer (MO) Review/Sign-Off - After the regulatory review, the protocol and informed consent will undergo a final MO review/sign-off. Final MO comments are issued upon completion of the review. These comments must be addressed before final DAIDS sign-off.

6.2.4. Final DAIDS Sign-Off - After the MO review/sign-off, the protocol and informed consent will be submitted to DAIDS-RAB via the RCC Regulatory group for sign-off on the final version of the protocol and informed consent.

6.3. Steps for Protocol Registration:

6.3.1. Clinical research sites are required to submit the DAIDS approved final version of the protocol and informed consent(s) along with the site-specific informed consent(s) to their IRB/EC and ministry of health and/or national IRB/EC, if applicable, for review and approval.

6.3.2. Upon receiving IRB/EC approval(s), clinical research sites will submit all required protocol registration documents to the PRO. Refer to Appendix 1

entitled, "Protocol Registration at a Glance" for a list of documents required for initial and amendment protocol registration.

6.3.3. The PRO will process the materials submitted for protocol registration within 10 business days from the date a complete submission is received at the PRO.

6.3.3.1. The PRO performs a detailed initial quality assurance review of the protocol registration documents submitted. These documents are reviewed for completeness and accuracy.

6.3.3.2. If problems are identified during the initial quality assurance review, a "request for materials" notification will be sent to the IoR and any additional personnel listed on the DAIDS Protocol Registration Checklist (i.e. study coordinator). This notification will outline the missing or corrected materials that must be submitted to the PRO. Missing or incorrect materials will stop a review and the review process will not continue until the missing or corrected materials are received at the PRO.

6.3.3.3. If no problems are identified during the initial quality assurance review, the site specific informed consent(s) is reviewed to ensure that all the required basic and additional informed consent elements are included.

6.3.4. Refer to the DAIDS Protocol Registration Policy and Procedure Manual for additional information regarding the protocol registration review process.

6.3.4.1. Notification of DAIDS approval/disapproval will be sent to the IoR and any additional personnel listed on the DAIDS Protocol Registration Checklist (i.e. study coordinator). A "disapproval" notification will outline the deficiencies in the site-specific informed consent(s) that must be revised and/or corrected.

6.3.4.2. Clinical research sites are required to submit the required protocol registration documents to the PRO for all protocol amendments after receiving IRB/EC approval(s). A clinical research site must receive DAIDS protocol registration approval prior to using the amended site-specific informed consent. Refer to Appendix 1 entitled, "Protocol Registration at a Glance" for a list of documents required for protocol registration of amendments.

6.3.4.3. Clinical research sites are required to submit documentation of IRB/EC Continuing/Annual Review and approval to the PRO within 30 days of final IRB/EC approval. Refer to the current DAIDS Protocol Registration Policy and Procedure Manual for additional information regarding IRB/EC Continuing/Annual Review.

6.3.4.4. Protocol registration approval does not authorize a clinical research site to begin enrollment of participants. Clinical research sites will be notified by the appropriate DAIDS scientific program(s) (i.e. Program/Project Officer), Operations Center or Data Management Center when enrollment may begin.

7.0 REFERENCE

U.S. Code of Federal Regulations, Title 45, Part 46
http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

U.S. Code of Federal Regulations, Title 21, Part 50
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm

Office for Human Research Protections
http://www.hhs.gov/ohrp/

RCC website – Protocol Registration Policy and Procedure Manual
http://rcc.tech-res-intl.com/DAIDS%20RCC%20Forms/HighlightOff_PROManual_v04b.pdf

8.0 INQUIRIES

Questions and comments regarding this policy may be directed to the OPCRO Policy Group at: NIAIDOPCROPOLICYGROUP@mail.nih.gov

9.0 AVAILABILITY

This policy is available electronically at the following URL:
http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch/Default.htm

The signed original is maintained in the OPCRO policy office.

10.0 CHANGE SUMMARY

Version #	Date	Replaces	Date of Revision	Rationale for Revision/Retirement
2.0	20 DEC 06	V 1.0	20 DEC 06	DAIDS Final Review
1.0	14 JUL 06	N/A	N/A	N/A

11.0 APPENDICES

Appendix 1 - Protocol Registration at Glance

12.0 APPROVAL

	Signature	**Program/Branch**	**Date**
Authorized By:	Richard Hafner		December 20, 2006
	Richard Hafner, MD Director	Office for Policy in Clinical Research Operations (OPCRO)	